TECHNOLOGY TRANSFER CENTER
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Anti-Cancer Agents That Inhibit Cell Motility, Angiogenesis, and Metastasis

Reference No. E-265-1999

Categories: Therapeutics-Cancer, various types
Keywords: Grb2, Src homology-2 (SH2) domain, antagonists, hepatocyte growth factor (HGF), vascular endothelial cell growth factor (VEGF)

Background:
The National Cancer Institute's Urologic Oncology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Grb2 SH2 domain antagonists as anti-cancer drugs.

Technology:
The Grb2 protein, through its SH2 domain, mediates growth factor driven cell motility *in vitro* and angiogenesis *in vivo*. This invention describes potent, highly selective antagonists of Grb2 SH2 domain binding that have been shown to block cell motility stimulated by several growth factors including hepatocyte growth factor (HGF) and vascular endothelial cell growth factor (VEGF). Because the ability of these growth factors to initiate increased cell motility is frequently linked to tumor metastasis, the antagonists described in this technology have the potential to improve cancer survival rates by inhibiting metastasis. Additionally, they potently inhibit HGF and VEGF-stimulated morphogenesis and angiogenesis. This discovery is significant because HGF's signaling pathway is frequently over-activated in numerous human cancers, including colon, gastric, breast, lung, thyroid and renal carcinomas, melanoma, several sarcomas as well as glioblastoma.

The small, synthetic Grb2 SH2 domain antagonists have already been shown to inhibit metastasis of melanoma and prostate cancer-derived tumor cells in mice. These results establish a critical role for Grb2 SH2 domain-mediated interactions during metastasis and support the efficacy of this class of compound in reducing the spread of solid tumors in humans.

R&D Status: *In vivo* and *in vitro* studies have been conducted on this technology.

IP Status: PCT Patent Application No. PCT/US2007/078494 filed 14 Nov 2007

Value Proposition:
- Potential to improve cancer survival rates by inhibiting cell motility, angiogenesis, and tumor metastasis
- Novel mechanism to reduce the spread of solid tumors and treat numerous types of cancers

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